

2. (Amended) The method of claim 1, wherein the first member of the fusion protein is an immunoglobulin subunit.

3. (Amended) The method of claim 1, wherein the first member is fused to the second member and the first member includes a subunit of a targeting molecule and the second member encodes a cell toxin.

Q¹
4. (Amended) The method of claim 1, wherein the first member includes a subunit of an immunoglobulin specific for a tumor antigen.

5. (Amended) The method of claim 4, wherein the tumor antigen is from the group consisting of carcinoembryonic antigen (CEA), a transferrin receptor, TAG-72, and an epidermal growth factor.

6. (Amended) The method of claim 1, wherein the second member is an RNase.

7. (Reiterated) The method of claim 6, wherein the RNase is RNase A.

Q²
8. (Amended) The method of claim 1, wherein the second member is angiogenin.

10. (Amended) The method of claim 2, wherein the immunoglobulin subunit of the fusion protein is a human antibody or antigen binding portion thereof.

Q³
11. (Amended) The method of claim 1, wherein the fusion protein is produced in the milk of the mammal at concentrations of at least about 0.5 mg/ml.

12. (Amended) The method of claim 1, wherein the fusion protein is produced in the milk of a transgenic mammal at concentrations of at least about 1.0 mg/ml.

13. (Amended) The method of claim 2, wherein the immunoglobulin subunit of the fusion protein is a humanized antibody or antigen binding portion thereof.

Q³
14. (Amended) The method of claim 1, wherein the transgene encoding the fusion protein is a nucleic acid which comprises:

- (a) a mammary epithelial specific promoter;
 - (b) a nucleotide sequence which encodes a signal sequence which can direct the secretion of the fusion protein;
 - (c) one or more nucleotide sequences which encode the fusion protein.
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15. (Cancel) An isolated nucleic acid construct, comprising
- (a) optionally, an insulator sequence;
 - (b) a mammary epithelial specific promoter;
 - (c) a nucleotide sequence which encodes a signal sequence which can direct the secretion of the fusion protein e.g., a signal from a milk protein;
 - (d) optionally, a nucleotide sequence which encodes a sufficient portion of the amino terminal coding region of a secreted protein, e.g., a protein secreted into milk, to allow secretion, e.g., in the milk of a transgenic mammal, of the fusion protein;
 - (e) one or more nucleotide sequences which encode the fusion protein; and
 - (f) optionally, a 3' untranslated region from a mammalian gene, e.g., a mammary epithelial specific gene (e.g., a milk protein gene).

In another aspect, the invention features a pharmaceutical or nutraceutical composition having an effective amount of fusion protein, e.g., an immunoglobulin-enzyme fusion protein as described herein, a pharmaceutically acceptable carrier.

In a preferred embodiment, the composition includes milk.

Q⁴
16. (Amended) A non-human transgenic mammal which includes a transgene that encodes a fusion protein, the transgene comprising: a mammary epithelial specific promoter, a nucleotide sequence which encodes a signal sequence which can direct the

Q 4
secretion of the fusion protein, and one or more nucleotide sequences encoding the fusion protein, wherein the fusion protein includes a first member and a second member, the second member is an enzyme produced in the milk of a transgenic mammal in active form, and the fusion protein is produced in the milk of the transgenic mammal at a concentration of at least about 0.1 mg/ml.

17. (Amended) The transgenic mammal of claim 16, which can produce the fusion protein into its milk at concentrations of at least about 0.5 mg/ml.--

Please add claims 18-35.

-- 18. (New) The method of claim 2, wherein the immunoglobulin subunit of the fusion protein is a chimeric antibody or antigen binding portion thereof.

19. (New) The method of claim 4, wherein the tumor antigen is a transferrin receptor.

Q 5
20. (New) The method of claim 1, wherein the first member of the fusion protein is directly fused to the second member.

21. (New) The method of claim 1, wherein the first member of the fusion protein is linked to the second member by a linker sequence.

22. (New) The method of claim 1, wherein the transgenic mammal is a goat.

23. (New) The method of claim 1, wherein the transgenic mammal is a cow.

24. (New) The transgenic mammal of claim 16, wherein the first member of the fusion protein is an immunoglobulin subunit.

25. (New) The transgenic mammal of claim 16, wherein the first member is fused to the second member and the first member includes the subunit of a targeting molecule and the second member encodes a cell toxin.

26. (New) The transgenic mammal of claim 16, wherein the first member of the fusion protein includes a subunit of an immunoglobulin specific for a tumor antigen.

27. (New) The transgenic mammal of claim 26, wherein the tumor antigen is from the group consisting of carcinoembryonic antigen (CEA), a transferrin receptor, TAG-72, and an epidermal growth factor.

28. (New) The transgenic mammal of claim 16, wherein the second member of the fusion protein is an RNase.

29. (New) The transgenic mammal of claim 28, wherein the RNase is RNase A.

30. (New) The transgenic mammal of claim 16, wherein the second member of the fusion protein is angiogenin.

31. (New) The transgenic mammal of claim 24, wherein the immunoglobulin subunit of the fusion protein is a human antibody or antigen binding portion thereof.

32. (New) The transgenic mammal of claim 24, wherein the immunoglobulin subunit of the fusion protein is a humanized antibody or antigen binding portion thereof.

33. (New) The transgenic mammal of claim 24, wherein the immunoglobulin subunit of the fusion protein is a chimeric antibody or antigen binding portion thereof.

Applicant : Michael D. Edge et al.
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Attorney ocket No.: 10275-137001

Q 5 34. (New) The transgenic mammal of claim 16, wherein the mammal is a goat.

35. (New) The transgenic mammal of claim 16, wherein the mammal is a cow.--
